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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER
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ART UNIT	PAPER NUMBER
1649	13

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Please find below and/or attached an Office communication concerning this application or
proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
08/779,460

Applicant(s)
Goddijn et al.

Examiner
Ousama Zaghmout

Group Art Unit
1649



☒ Responsive to communication(s) filed on Jan 7, 1997

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 35 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) 1-24 is/are pending in the application

Of the above, claim(s) 2, 3, and 16-24 is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1 and 4-15 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been
☐ received.

☐ received in Application No. (Series Code/Serial Number) _____

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 13

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

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Status of application

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1649.

Election/Restriction

This application contains claims directed to the following patentably distinct species of the claimed invention:

- A. Claims 1-5, 9-24 are drawn to transgenic plants that overexpress trehalose a chimeric gene in the sense orientation, transformed plant cells and plants, and methods for their use, classified in class 800, subclass 205 for example.
- B. Claims 1, 4-5, 9-15 are drawn to transgenic plants that overexpress trehalase chimeric gene, transformed plant cells and plants, and methods for their use, classified in class 800, subclass 205 for example.
- C. Claims 1, 4-15 are drawn to the use of trehalase inhibitor comprises validamycin A and 86 KD protein of the cockroach, classified in class 800, subclass 205 for example.

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D. Claims 1,4-5, 8-15 are drawn to transgenic plants that underexpress trehalose chimeric gene in the antisense orientation, transformed plant cells and plants, and methods for their use, classified in class 536, subclass 24.5 for example.

The inventions are distinct, each from the other because each is drawn to biochemically, and molecularly divergent products and processes not required by the other.

The invention of group A is drawn to transgenic plants that overexpress trehalose chimeric gene in the sense orientation, not required by invention of group B which is directed toward the overexpression of trehalase, the enzyme which degrades trehalose. Also, invention of group A is not required by invention of group C which is directed toward the use trehalase inhibitor of insect origin, or by invention of group D which is directed toward decreasing the amount of trehalose in the tissue.

The invention of group B is drawn to overexpressing trehalase, not required by inventions of groups A and D.

The invention of group C is drawn toward increasing the accumulation of trehalose by treating tissues with trehalase inhibitor, not required by inventions of groups A, B and D. Furthermore, this inhibitor could be made by a process other than the use of antisense construct of group D, such as chemical synthesis.

The invention of group D is drawn to underexpressing trehalase by transforming with construct containing trehalose synthesizing gene in the antisense orientation, not required by inventions of groups A, B and C.

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Inventions of groups C and D are related as process of making and product made. The inventions can be shown to be distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case, the product as claimed in group C can be made by materially different process such as chemical synthesis.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their divergent subject matter, classification, and fields of search, restriction for examination purposes as indicated is proper.

During a telephone conversation with Mr. Clifford J. Mass on April 20, 1998 a provisional election was made with traverse to prosecute the invention of group ~~C~~^D claims 1, 4-15. Affirmation of this election must be made by applicant in responding to this office action. Other claims were withdrawn from further consideration by the examiner, 37CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR.148(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of the inventorship must be accompanied by a diligently-filed petition under 37 CFR 1.48 (b) and the fee required under 37 CFR 1.17(h).

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Claim Rejections-35 U.S.C. 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 11 rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The plants containing trehalose, as claimed, have the same characteristics and utility as those found naturally and therefore do not constitute patentable subject matter. See *American Wood v. Fiber disintegrating Co.*, 90 U.S. 566 (1974), *American Fruit Growers v. Brogdex Co.*, 283 U.S. 2 (1931), *Funk Brothers Seed Co. V. Kalo Inoculant Co.*, 33 U.S. 127 (1948), *Diamond v. Chakrabarty*, 206 USPQ 193 91980. Amendment of the claims to insert -- following treatment with trehalase inhibitor -- after "trehalose" would overcome the rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1st Paragraph

Claims 1, 4-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inhibiting trehalase degradation by applying the trehalase inhibitor validamycin A, does not reasonably provide enablement for claims drawn to the production of plants having the genetic information required for production of trehalose by inhibiting trehalase activity by incubating with the inhibitor validamycin A and by transforming with the nucleotide sequence which encodes the trehalase inhibitor after isolating it from cockroach. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The specification only provides guidance regarding the use of the trehalase inhibitor validamycin A to allow trehalose accumulation in tobacco and potato. Applicants provide no example for cloning of the nucleotide sequence of the trehalase inhibitor from cockroach nor its expression in any transgenic plants to show if it causes the accumulation of trehalose. Furthermore, the instant disclosure does not disclose any step on how the mutagenesis, modification, the alteration of the coding sequence around the translation initiation site to accommodate Kozak consensus sequence, or the cloning and sequencing of the nucleotide sequence of the trehalase inhibitor from cockroach will be performed. The instant disclosure fails

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to teach the factors which are essential for successfully expressing trehalase inhibitor gene from cockroach. Furthermore, modification of the coding sequence to enhance the expression of non-plant gene in plants requires many steps which they have not be addressed in the instant disclosure which include: changes in the localization of the regions of A+T richness to resemble the plant introns, and the optimization of the potential plant polyadenylation signal sequences, ATTTA sequences to avoid any destabilization of the mRNA in the plant. In addition, the introduction of single genes which encode a single enzyme in a metabolic pathway may be insufficient to effect the desired phenotype in the transformed plants, due to feedback inhibition, improper levels of various substrates or precursors, or the influence of other factors on the phenotype. Smith et al. failed to observe the desired retardation of fruit softening in tomato plants transformed with antisense DNA to the polygalacturonase gene, presumably due to the involvement of other unknown factors (Smith et al. Nature. 1988. Vol. 334 (25): 724-726. see, e.g., page 725, paragraph bridging the columns). Taken together, the instant disclosure lacks the proper and sufficient guidance to enable the claims as set forth.

Furthermore, The expression of foreign genes in transgenic plants is unpredictable, as shown by Matzke and Matzke (Plant Physiology. 1995. 107: 679-685). Matzke and Matzke teach that transgenes often become methylated in both plant and animal cells (Plant Physiology. 1995. 107: 679-685) in page 68, lines 14 to 19. Matzke and Matzke teach that transgenes are recognized as "foreign" by a genomic immune function (page 681, lines 18 to 19). Matzke and

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Matzke termed this type of gene silencing as co-suppression or sense-suppression which involves the coordinate silencing of the transgene with the homologous endogenous gene.

The instant disclosure failed to address a solution for these problems. Taken together, the instant disclosure lacks the proper and sufficient guidance to enable the claims as set forth. Applicant's disclosure does not provide sufficient representative examples for the use and/or construction of transgenic plants that express the nucleotide sequence of the trehalase inhibitor from cockroach .

Given the claim breadth, unpredictability, and the lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to generate transgenic plants that express the cloned nucleotide sequence of the trehalase inhibitor from cockroach and whether trehalose will be accumulated in the transgenic plants.

2nd Paragraph

Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9 is indefinite in its recitation of the term "above". The term "above" in claim 9 is a relative term which renders the claim indefinite. The term "above" is not defined by the specification.

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The specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. For more details on limitations following the phrase which are part of the claimed invention, see MPEP § 2173.05(d).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 6, 9-10, and 13-14 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Kendall et al. (Phytochemistry, 1990. Vol. 29: 2525-2528).

The claimed inventions read on Kendall et al. as follows:

Kendall et al. teach the use of validamycin A as a specific trehalase inhibitor (abstract). Kendall et al. teach the accumulation of trehalose in tissue treated with validamycin A at a concentration of 100 nM and 10 mM (Fig. 2, page 2526). Kendall et al. teach the use of a plant, or a plant part for extracting trehalose (Material and Methods section, page 2527). Kendall et al. teach a process of forced extraction from said plant or plant part (page 2527 under quantitative

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analysis of trehalose breakdown of Material and Method section). All elements of the claims are found in the reference.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter *as a whole* would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 4-6, 8-15 are rejected under 35 U.S.C 103 (a) as being unpatentable over Kendall et al. (Phytochemistry. 1990. Vol. 29: 2525-2528) in view of Belknap et al. (American Potato Journal. 1994: Vol. 7: 285-296).

The claims are drawn to a process intended to enhance the accumulation of trehalose in tissues by treating plant with the trehalase inhibitor such as validamycin A where the plant is *Solanum tuberosum* and its microtubers.

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Kendall et al. teach the use of various concentrations of validomycin A (10^{-11} - 10^{-5} M) in treating plant tissues to cause the accumulation of trehalose (Figure 1, page 2526).

Kendall et al. do not disclose or expressly teach the use of validomycin A on cause the accumulation of trehalose in *Solanum tuberosum* plants and their microtubers.

Belknap et al. teach the usage of potato in experiments. Furthermore, Belknap et al. teach a reliable procedure for the production of transgenic potato plants (abstract).

Kendall et al., and Belknap et al., are combinable because they are from a similar problem solving area, viz., production of plants with desirable traits.

At the time of the invention, it would have obvious to a person of ordinary skill in the art to combine the use of potato plants and microtubers of Belknap et al., with trehalase inhibitor validomycin A of Kendall et al. The motivation for doing so would have been to enhance the accumulation of trehalose in plant. The disaccharide trehalose is a stress-protective and preservative agent in plants.

Therefore, it would have been obvious to combine Kendall et al., and Belknap et al. to obtain plants and process of increasing trehalose production in plant as specified in claims 1, 4-6, 8-15. Thus the claimed invention would have been prima facie obvious as a whole to one of ordinary skill in the art at the time the invention was made, especially in absence of evidence to the contrary.

Prima Facie-Obyiousness

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It is the Examiner's position that all elements of the applicant's invention with respect to the claims are instantly disclosed or fully envisioned by the teaching of the references cited above.

Claims 1, 4-5, 7-15 are rejected under 35 U.S.C 103 (a) as being unpatentable over Belknap et al. (American Potato Journal. 1994: Vol. 7: 285-296) in view of Hayakawa et al. (The Journal of Biological Chemistry. 1989. Vol. 204: 16165-16169), and Ausubel et al. (Short Protocols in Molecular Biology. Published by Greene Publishing Associates and Wiley-Interscience. John Wiley & Sons. 1989).

Claims 1, 4-5, 7-15 are drawn to enhance the accumulation of trehalose in tissues by transforming with gene encodes the trehalase inhibitor isolated from American cockroach.

Belknap et al. teach the usage of potato in experiments. Furthermore, Belknap et al. teach a reliable procedure for the production of transgenic potato plants (abstract).

Belknap et al. do not disclose or expressly teach the accumulation of trehalose in plants by transforming with the gene which encodes the trehalase inhibitor from American cockroach.

Hayakawa et al. teach the amino acid composition of the trehalase inhibitor from cockroach (Table II, page 16168).

Ausubel et al. Teach the molecular techniques for the cloning , sequencing and making constructs (Chapters 6 and 7).

Belknap et al., Hayakawa et al., and Ausubel et al., are combinable because they are from a similar problem solving area, viz., the use of molecular genetics to identify the functions of genes.

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At the time of the invention, it would have obvious to a person of ordinary skill in the art to combine the making of the plant expression vector containing the gene which encodes trehalase inhibitor of Kendall et al. using the molecular tools of Ausubel et al. with the procedure for producing transgenic plants of Belknap et al. The motivation for doing so would have been to enhance the accumulation of trehalose in plant. The disaccharide trehalose is a stress-protective and preservative agent in plants.

Therefore, it would have been obvious to combine Belknap et al., and Kendall et al. to obtain the invention as specified in claims 1, 4-5, 7-15. Thus the claimed invention would have been prima facie obvious as a whole to one of ordinary skill in the art at the time the invention was made, especially in absence of evidence to the contrary.

Prima Facie-Obviousness

It is the Examiner's position that all elements of the applicant's invention with respect to the claims are instantly disclosed or fully envisioned by the teaching of the references cited above.

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Future Correspondence

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Ousama M-Faiz Zaghmout whose telephone number is (703) 308-9438. The Examiner can normally be reached Monday through Friday from 7:30 am to 5:00 pm (EST).

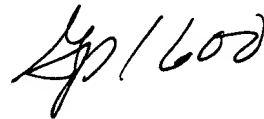
If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Douglas Robinson, can be reached on (703) 308-2897. The fax phone number for the group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to THE MATRIX CUSTOMER SERVICE CENTER whose telephone number is (703) 308-0196.

Ousama M-Faiz Zaghmout Ph.D
May 9, 1998

A handwritten signature in black ink, appearing to read "D. Robinson", with a long horizontal flourish extending to the right.

DOUGLAS W. ROBINSON
SUPERVISORY PATENT EXAMINER

Handwritten text in black ink, possibly initials or a reference number, appearing to be "Sp/602".